

Core Oncology Outcome Strategies: Do They Offer an Opportunity for Simplicity and Consistency, or Pose a Risk to Comprehensive Understanding of Patient Experiences?

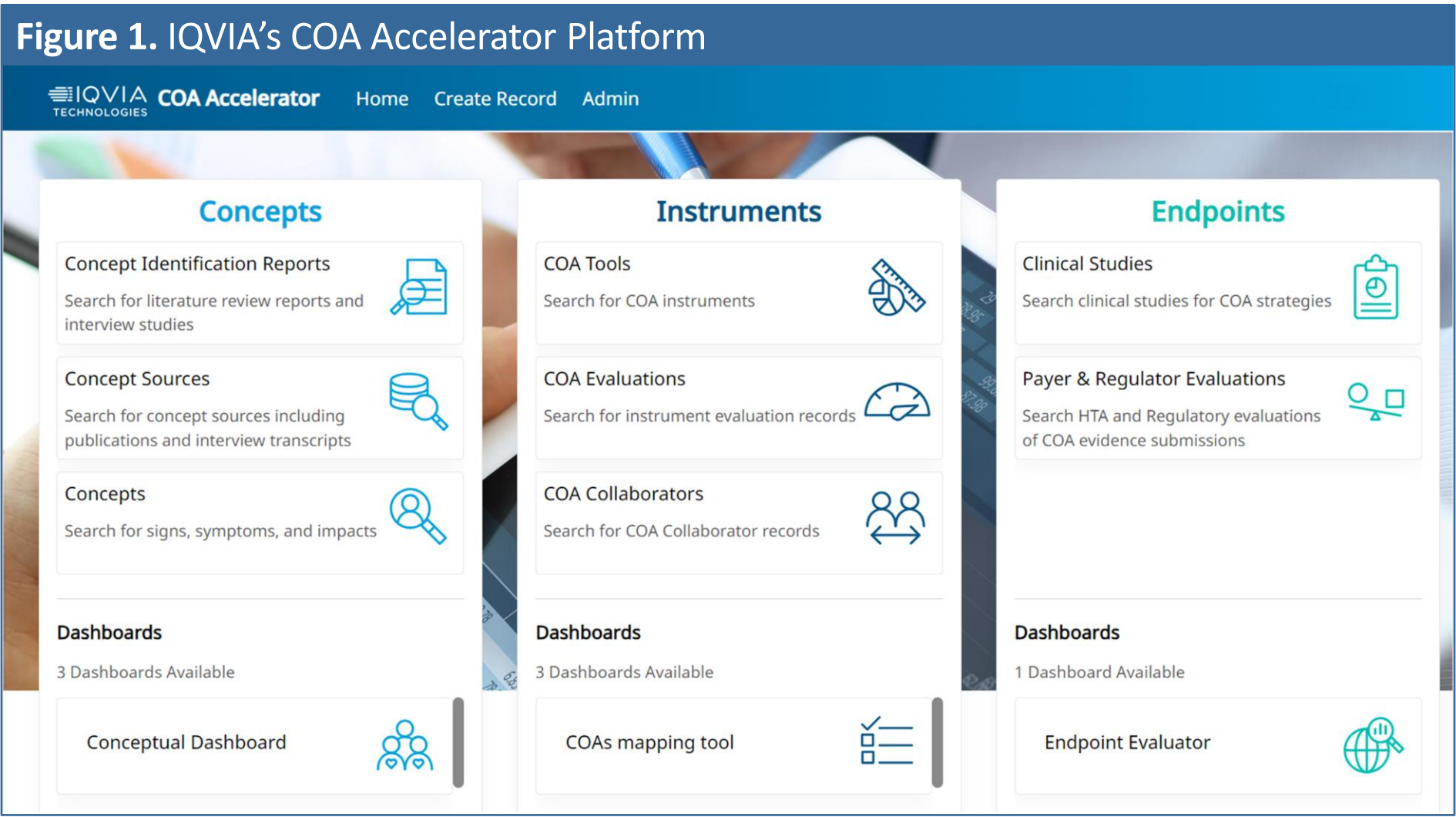
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Background & Objectives

- The FDA proposes a core set of clinical outcomes to define treatment benefit across oncology indications during drug/biologic development: symptoms, symptomatic adverse events, physical and role functioning
- While there is appeal in such consistent approach, it somewhat conflicts with the concept of patient-focused drug development (PFDD) which highlights the importance of comprehensively understanding and measuring the most important concepts for a specific target population
- This study examined conceptual models from 5 oncology indications, showing patient-relevant concepts for defining disease burden, to explore whether the FDA's core set of outcomes were included in all 5
- Further, it was examined whether a general measurement approach could be considered across indications

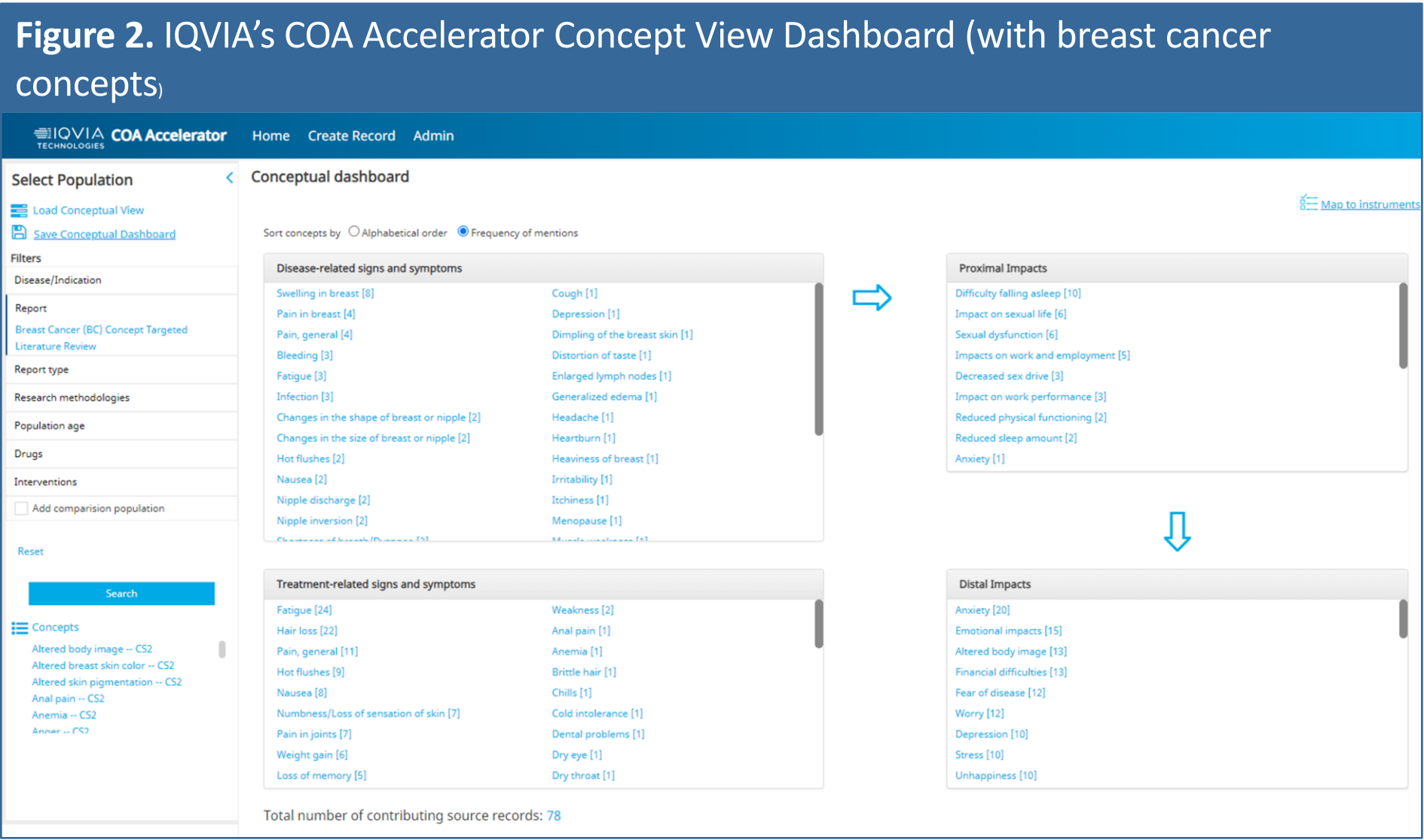
Methods

- IQVIA's COA Accelerator (COAA) was used to auto-generate conceptual models based on existing published qualitative research studies in 5 indications: melanoma, breast, prostate, head & neck and hepatocellular carcinoma
- Using the concept view dashboard, the conceptual models were overlaid to evaluate similarities and differences across the five sets of outcomes
- The concepts in common across five, four, three and two conceptual models were listed and analysed



Identification of oncology concepts

- Concepts related to the five oncology indications extracted from COA Accelerator originate from targeted literature reviews (TLRs). These TLRs focus on disease-related signs and symptoms, treatment-related signs and symptoms and impacts of the disease. The articles included in the TLRs are largely focused on reports of the patient experience as described by patients themselves, including methodologies such as qualitative interviews or focus groups
- COA Accelerator is a platform that allows TLR data, among other types of data, to be curated and organized in a structured way – one of the displays being the conceptual dashboard (**Figure 2**)



Results

- The total number of concepts identified for each of the five indications is presented in **Table 1**

Table 1. Number of individual concepts identified per indication				
Indication	Disease-related signs & symptoms	Treatment-related signs & symptoms	Unique signs & symptoms (disease or treatment-related)	Impacts
Melanoma	33	43	12	97
Head and neck cancer	32	51	16	64
Hepatocellular carcinoma	51	39	26	42
Prostate cancer	63	65	20	61
Breast cancer	42	69	24	62

- Concepts were categorized into disease-related signs/symptoms, treatment-related signs/symptoms and impacts (proximal and distal). There were at least 32 concepts per category, up to a maximum of 97 individual concepts
- Each indication had at least 100 individual concepts identified, which highlights how varied the patient experience is for these patients
- One interesting finding is that, with the exclusion of hepatocellular carcinoma, all other indications had more treatment-related concepts identified compared to disease-related concepts
- Furthermore, impacts of all types were also numerous, thus hinting at the importance of also considering more distal concepts as part of a holistic patient experience measurement strategy
- In addition to the total number of concepts identified, COA Accelerator also extracts information about prevalence of signs/symptoms/impacts where it is reported in the literature. **Table 2** shows the three most prevalent concepts for each indication in each category were identified (**Table 2**)

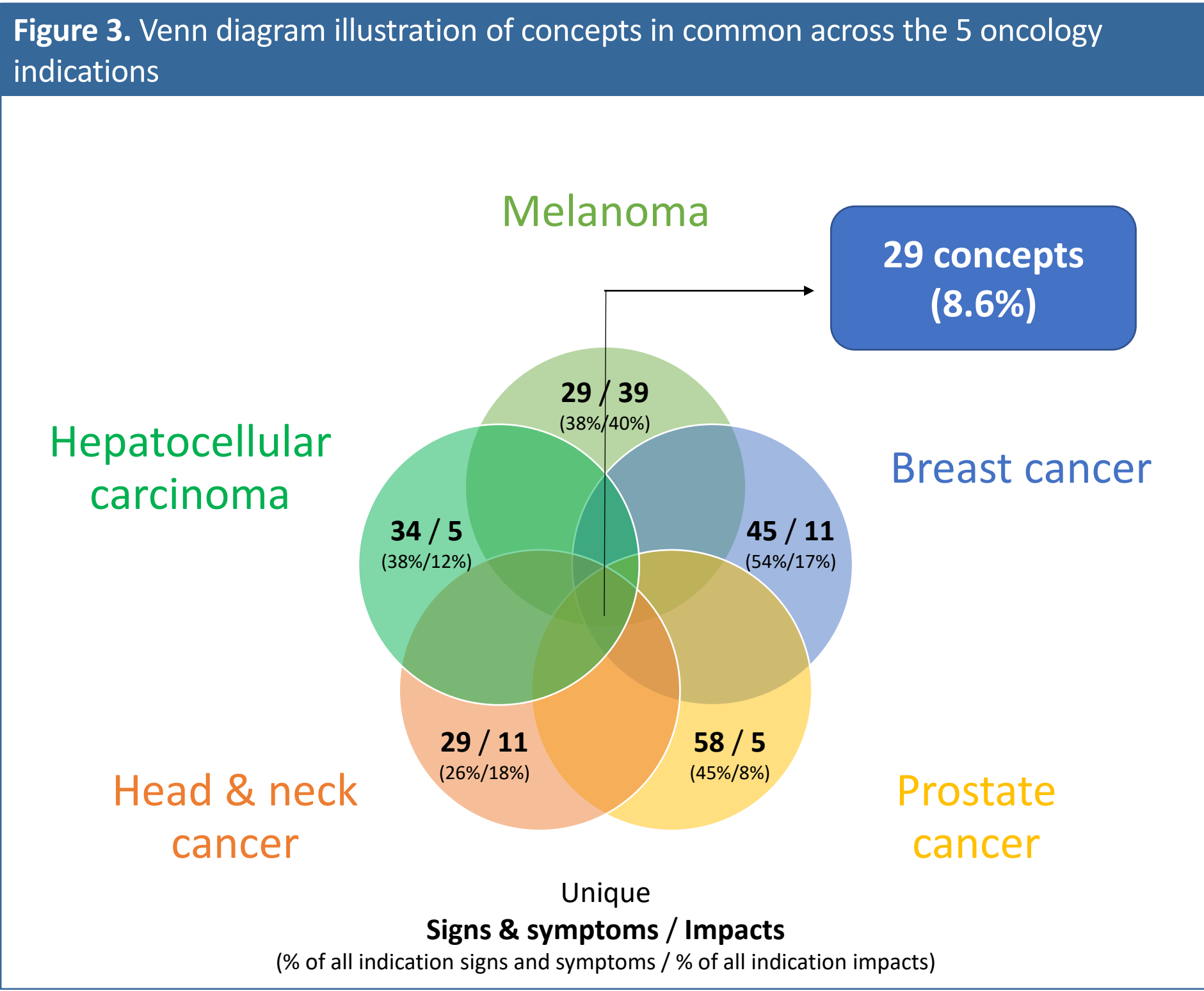
Table 2. Identified concepts with highest reported prevalence, per indication			
Indication	Disease-related signs & symptoms	Treatment-related signs & symptoms	Impacts
Melanoma	Skin lesions (77%) Skin lumps/nodules (68%) Altered skin pigmentation (59%)	Fatigue (90%) Diarrhea (70%) Constipation (70%)	Impact on family role function (90%) Impact on social life (90%) Worry about disease(66%)
Head and neck cancer	Difficulty swallowing (74%) Difficulty speaking (74%) Breathing abnormality (74%)	<i>Prevalence data for treatment-related side effects not reported in the literature</i>	Memory impairment (80%) Depression (49%) Emotional impacts (49%)
Hepatocellular carcinoma	Fatigue (100%) Pain in abdomen (95%) Dry mouth (95%)	Sexual dysfunction (75%) Muscle atrophy (60%) Skin abnormalities (50%)	Worry (64%) Impact on voice (10%) Physical impacts (10%)
Prostate cancer	Sexual dysfunction (100%) Decreased sex drive (100%) Erectile dysfunction (100%)	Fecal urgency (11%) Allergic reaction (9%) Bruising (6%)	Difficulty with self care/ADLs (81%) Reduced sleep amount (76%) Worry (76%)
Breast cancer	Fatigue (100%) Pain and tenderness (49%) Heaviness (45%)	Fatigue (100%) Nausea (70%) Shortness of breath/Dyspnea (82%)	Depression (86%) Memory impairment (100%) Difficulty concentrating (97%)

Footnote: numbers in parenthesis represent the highest reported prevalence for the concept, across all sources mentioning the concept.

- Besides some concepts in common across indications, there was significant variability in the most prevalent concepts per indication
- The prevalence rates for the top prevalent concepts also varied considerably, with some concepts being reported by all patients, to some concepts being reported by less than 10% of patients, for some indications – suggesting variability of the patient experience not only across diseases, but to some extent within the same indication as well. It should be noted that prevalence data was only available for 12% to 57% of the articles extracted

Identification of concepts in common across indications

- There were a total of 29 concepts identified that were in common across the five oncology indications, representing 8.6% of the total individual concepts identified (**Figure 3**)
- All of the 29 concepts identified as overlapping were mapped to the core concepts proposed by FDA: 5 represent symptomatic adverse events, 2 represent disease related symptoms, 5 represent physical function and 19 represent role function
- While the *role function* category had the most concepts, some of the entries correspond to broad non-physical impacts that may or may not be correlated with role functioning
- An interesting finding was that the biggest similarities were found on more distal concepts compared to proximal concepts like signs and symptoms



- Another interesting find was that only fatigue and nausea were identified as common concepts in the *disease-related symptoms* category

Table 3. Concepts found in common across one to five oncology indications			
Number of indications	Signs & symptoms	Impacts	Total concepts
Common across 5 indications	5	24	29
Common across 4 indications	15 (+10)	32 (+8)	47 (+18)
Common across 3 indications	39 (+24)	54 (+22)	93 (+46)
Common across 2 indications	84 (+45)	71 (+17)	155 (+62)
Appearing in just 1 indications	195	71	266

Footnote: numbers in parenthesis represent the additional number of concepts from the previous row.

Table 4. Concepts in common across indications, organized according to FDA's Core Patient-Reported Outcomes guidance categories			
Symptomatic adverse events	Disease related symptoms	Physical function	Role function
Fatigue Loss of appetite Nausea General pain Constipation	Fatigue Nausea	Reduced physical functioning Physical impacts Decreased mobility Difficulty falling asleep Reduced sleep quality	Unhappiness Emotional impacts Fear Depression Difficulty with self-care / activities of daily living Impact on social life Impacts on work and employment Impact on family life Financial difficulties Uncertainty Anxiety Stress Worry Anger Impact on relationship with others Difficulty concentrating Altered body image Cognitive impairment Fear of disease

Footnote: the fifth category of outcomes defined by the FDA guidance is "overall side effect impact summary measure" was not included as no individual concept can be matched to this overarching category. However, treatment-related symptoms were identified in all 5 indications. These varied between indications, supporting the premise of an overall assessment of overall side-effect impact.

- A significant observation is that the vast majority of the symptoms that were identified as the most prevalent for each individual indication were not found to be in common across the cancer types evaluated
- Distal concepts like physical function, but especially role functioning, were more frequently found to be in common – an area where historically the FDA has not granted as many labelling claims
- While these findings may unveil some interesting findings, it is important to note that the concepts identified are limited to 5 of the most commonly occurring cancers, and that the source of concepts is the literature; using novel, primary concept elicitation interviews employing a consistent discussion guide would be an ideal complement to this analysis

Conclusions

- Overall, there was little overlap in the total number concepts across the 5 sample indications (only 8%)
- The most prevalent disease-related symptoms are not found to be in common across the oncology indications evaluated; besides, only two disease-related symptoms were overlapping – raising questions on the utility of a core outcome for this dimension of the patient experience
- The overlap of concepts is very rich in impacts, and there are many non-physical impacts that are not easily categorized as role functioning – an emotional function outcome could be considered
- Careful consideration is advised when proposing a generic approach to measuring the patient experience in oncology – the inclusion of disease-specific measures that more comprehensively and accurately capture the indication-specific patient experience is recommended

References

1.FDA, Core Patient-Reported Outcomes in Cancer Clinical Trials, Draft Guidance for Industry, June 2021

Acknowledgments

The authors would like to thank Matt Reaney for scientific and editing input in the writing of this poster.